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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,763	QI ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-11 and 18-31* is/are pending in the application.

4a) Of the above claim(s) *12,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-11 and 18-31* is/are rejected.

7)☒ Claim(s) *24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/12/08 has been entered.

Claims 1, 2, 4, 6, 8, 11, 18, and 19 are amended.

Claims 20-31 newly added.

Claims 1, 2, 4-12, 14, 15, and 18-31 are presently pending.

Election/Restrictions

Claims 1, 2, 4-11, and 18-31 are presently eligible for consideration for the elected invention and species, with the rejoinder of SEQ ID NO: 2, as it is noted that the other species are no longer specifically claimed.

Claim Objections

In light of the amendments, the objections to Claims 6, 8-11, and 18 under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple-dependent claim, are withdrawn.

In light of the amendment, correcting the terminology used for CD8 alpha chain, the objections to Claims 2 and 4 are withdrawn.

Claim 24 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 24 indicates that the CD8 alpha chain is a fusion protein, and hence, is not properly dependent from the claim(s) from which it depends.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Applicant is advised that should claim 8 be found allowable, claims 11 and 18 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 11 and 18 each require specific effects to obtained with the vector of Claim 8, when a cell is transformed with the virus, however, the effects are taught in the specification to be inherent in the vector composition itself, and not to require a distinct structure. Hence, the scope of the composition of Claims 11 and 18 is the same as that of Claim 8, despite a slight difference in wording.

Applicant is advised that should claim 26 be found allowable, claims 29 and 30 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 11 and 18 each require specific effects to obtained with the vector of Claim 8, when a cell is transformed with the virus, however, the effects are taught in the specification to be inherent in the vector composition itself, and not to require a distinct structure. Hence, the scope of the composition of Claims 11 and 18 is the same as that of Claim 8, despite a slight difference in wording.

New Matter Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Separate Expression Requirement

Claims 1, 2, 4-11, and 18-19 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for comprising new matter. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In order to curtail frivolous argument, and make the issue crystal clear, the present rejection on the basis of new matter, within the broader classification of written description. Such rejections are the original basis in which the written description developed. The rejection is properly applied when there is no specific contemplation of an amended claim limitation in the original specification and/or original claims. Such does not require any analysis of the prior art, as it rests on the basis as to whether Applicant constructively reduced the invention to practice at the time of filing.

Claim 1, and its dependent claims, as listed above, encompass a CD8 alpha-chain coding sequence, and a second sequence encoding a molecule of interest, each linked to control elements directing a generic separate expression of the CD8 alpha chain from that of the molecule of interest.

The specific contemplation of such expression control elements directing separate expression of the two coding sequences is simply not contemplated. Such is not found to be contemplated as the Examiner cannot explicit or implicit contemplation of such in the specification. To wit, separate expression may be found to be "separate" in several manners. For example, the expression may occur at separate times, or it may be in separate cell types, or it

may be separate because translation occurs from separate promoters, or it may be separate because the sequences are separated in expression due to separate translational control elements on a single transcript. Nowhere is this fleshed out in the specification. Moreover, the specification does describe embodiments where the therapeutic molecule is concatenated with the CD8 (paragraph 007, describing antibody binding sites linked to the CD8 alpha chain extracellular domain). However, nowhere is such embodiment excluded from being in the invention, yet it definately cannot be separately expressed.

Hence, due to the number of ways in which "separate expression" can be interpreted, the Artisan would not be able to determine that Applicant had possession of the breadth of the claimed invention at the time of invention.

Further, it is noted that it is Applicant's duty to disclose their support and not the Examiner's duty to find such support.

Response to Argument – New Matter, Separately Expressed

Applicant's argument of 4/14/08 has been fully considered but is not found persuasive.

Applicant argues that support is found in paragraph 0014, "for example", and paragraph 0016, reviewing several expression vectors and requirements for transcriptional regulatory nucleic acids operably linked (p. 7, paragraph 1).

Such is not persuasive. Paragraph 0014 is the only sort of statement which could be construed as even related in any way to the new limitation, yet it is also clear from the context of the paragraph that the separate expression is obtained in such paragraph due to separate expression vectors, not a single expression vector with separate transcription and translation regulatory sequences. Still further, neither paragraph cited addresses translational regulatory

elements, or any other basis addressed above. Finally, at best, obviousness could be found between the paragraphs cited to obtain the generic limitation, but obviousness does not supplant the need for possession.

Non-Fusion Protein Requirement

Claims 20-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for comprising new matter. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In order to curtail frivolous argument, and make the issue crystal clear, the present rejection on the basis of new matter, within the broader classification of written description. Such rejections are the original basis in which the written description developed. The rejection is properly applied when there is no specific contemplation of an amended claim limitation in the original specification and/or original claims. Such does not require any analysis of the prior art, as it rests on the basis as to whether Applicant constructively reduced the invention to practice at the time of filing.

Claims 20-31 require that the CD8 alpha chain not be a fusion protein. The specification does not provide any disclosure that such was the contemplated invention, and in fact, actually discloses that it can be fusion, utilizing distinct transmembrane domains, as is further indicated in Claim 24. Moreover, no disclosure is given about any other form of fusion or absence thereof in the original disclosure and claims.

Hence, the Artisan could not determine that Applicant was in possession of only any CD8 alpha chain comprising the extracellular domain, without being fused to another protein. There is simply no discussion to indicate that Applicant possessed such as their invention at the time of filing.

Further, it is noted that it is Applicant's duty to disclose their support and not the Examiner's duty to find such support.

Response to Argument – New Matter, Not a Fusion Protein

Applicant's argument of 4/4/08 has been fully considered but is not found persuasive.

Applicant argues that paragraph 0068 provides support for the alpha chain of CD8 not being a fusion protein (p. 7, paragraph 3).

Such is not persuasive. The limitation clearly does not evince possession of a generic non-fusion protein being considered to be part of the invention, but instead, given the context that the previous paragraph discusses making fusions with the transmembrane domain of another protein, and further that the specific paragraph describes the "non-fusion" as simply being a deletion of the CD8 alpha intracellular membrane domain, the Artisan would not consider Applicant to have excluded other fusions, particularly in the instance of a CD8-alpha proteins which delete more than the intracellular domain, but instead only comprise a soluble form of the extracellular domain. There is simply no way the Artisan would understand the cited paragraph to provide evidence of possession of the breadth of invention claimed. Instead the cited paragraph provides, at best, evidence of support only for a generic truncated CD8-alpha lacking its intracellular domain, which is further not a fusion protein.

Aruffo Reference Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, and 19 remain rejected, and Claims 8, 9, 10, 11, and 18 are newly rejected, under 35 U.S.C. 102(b) as being anticipated by US Pat. No. 5,540,926 to Aruffo, et al., as further evidenced by WO 04/042346 to Wohlgemuth, et al. and the previously attached SEQUENCE COMPARISON 1 OF 9/6/06, for reasons necessitated by the amendments, as demonstrated by e.g., U.S. Patent No. 5,851,806 to Kovesdi.

Aruffo teaches the preparation of soluble GP39, wherein the GP39 is linked to human CD8-alpha which minimally comprises its extracellular domain (e.g., col. 8, paragraph 5). Such proteins are taught to be made from nucleic acids transformed into a host cell which comprises an operatively linked promoter, and inherently must also comprise the translational control elements, otherwise the proteins would not be able to be translated (e.g., col. 7, paragraph 4). Moreover, the functional portion of the CD8-alpha chain in this case is that functional portion for tagging the GP39.

With regard to claim 19, Aruffo also teaches the use of plasmids and adenoviral vectors (col. 7, paragraph 3).

Further, as evidenced by Wohlgemuth, the nucleotide sequence is 100% identical to Applicant's claimed sequence for human CD8 alpha (See Attached SEQUENCE COMPRISON 1 OF 9/6/06, which demonstrates the sequence identity).

Still further, with regard to separate expression elements, Aruffo teaches placing the coding sequence of the GP39-CD8alpha into expression vectors which also comprise selection markers under separate expression elements (e.g., cols. 6-7 , paragraph bridging). Such selection marker coding sequences are nucleic acids of interest in selecting for the cells growing the vector and hence, the limitations of the claim are met. Morever, the same goes for making the replication defective adenoviral vectors, as demonstrated by, for example U.S. Patent No. 5,851,806, (e.g., EXAMPLES), wherein replication defective adenoviral vectors are made as plasmids.

Response to Argument – anticipation, Aruffo

Applicant's argument of 4/14/08 has been fully considered but is not found persuasive.

Applicant argues that the amendment, requiring separate expression, precludes fusion proteins (p. 9, penultimate paragraph).

Such is not persuasive. The separate expression only requires separate expression, and is not the exclusion of a fusion protein.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, and Claim 19 remain rejected, and Claims 8-11 and 18 are newly rejected, under 35 U.S.C. 103(a) as being unpatentable over US Pat. No. 5,540,926 to Aruffo, et al., and US Pat. No. 6,193,980 to Efstathiou, et al., as further evidenced by WO 04/042346 to Wohlgemuth, et al. and the previously attached SEQUENCE COMPARISON 1 OF 9/6/06, for reasons of record, and as described below for reasons necessitated by the amendments.

As shown above, Aruffo teaches the various aspects of each claim. Moreover, Aruffo teaches that the protein may be grown in any mammalian cell (e.g., col. 7, paragraph 3). However, Aruffo does not teach the aspect of using a replication defective herpes virus vector.

On the other hand, Efstathiou teaches replication defective herpes simplex virus comprising heterologous inserts for producing long-term infection and protein production in, *inter alia*, the sensory neurons of the dorsal root ganglia (e.g., col. 1, paragraph 5). Moreover, one specific construct made places the transcription of a selection gene in opposite direction from that of the gene of interest (in our case, CD8) (e.g., EXAMPLE 1). Lastly, it is noted that these vectors are typically made by working with plasmid forms which are then packaged (e.g., EXAMPLES).

Hence, at the time of invention, it would have been obvious to modify the vectors of Aruffo with the HSV vectors Efstathiou to arrive at the claimed invention. The artisan would have been motivated to do so in order to express the transgene for long terms, in dorsal root ganglia cells. The Artisan would also have had a reasonable expectation of success, Aruffo had demonstrated the protein's production, and Efstathiou had demonstrated that the vectors were useful for protein production in dorsal root ganglia.

Response to Argument – Obivousness, Aruffo and Efstathiou

Applicant's argument of 4/4/08 has been fully considered but is not found persuasive.

Applicant argues that the cited art fails to overcome the requirement for separate expression (p. 8, paragraph 2).

Such is not persuasive. Under the modified basis applied, it is clear that the Art still makes the claims obvious.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, and Claim 19 remain rejected, and Claims 8-11 and 18 are newly rejected, under 35 U.S.C. 103(a) as being unpatentable over US Pat. No. 5,540,926 to Aruffo, et al., and US Pat. No. 6,509,150 Salvetti, et al., as further evidenced by WO 04/042346 to Wohlgemuth, et al. and that attached SEQUENCE COMPARISON 1 OF 9/6/06, for reasons of record, as modified below due to the amendments.

As shown above, Aruffo teaches the various aspects of each claim. Moreover, Aruffo teaches that the protein may be grown in any mammalian cell (e.g., col. 7, paragraph 3). However, Aruffo does not teach the aspect of using a replication defective herpes virus vector.

On the other hand, Salvetti teaches adenoassociated viral vectors comprising heterologous inserts with improved efficiency, and may be for specific localization of

intergration of the vector (ABSTRACT; col. 6, last paragraph). Moreover, in specific examples, the vector made includes separate genes for selection (e.g., FIGURES 7 and 9).

Hence, at the time of invention, it would have been obvious to modify the vectors of Aruffo with the AAV vectors of Salvetti to arrive at the claimed invention. The artisan would have been motivated to do so in order to produce vectors with improved efficiency, for producing pharmaceutical proteins. The Artisan would also have had a reasonable expectation of success, Aruffo had demonstrated the protein's production, and Salvetti had demonstrated that the vectors could be used for specific integration (EXAMPLES).

Response to Argument – Obviousness, Aruffo and Salvetti

Applicant's argument of 4/4/08 has been fully considered but is not found persuasive.

Applicant argues that the cited art fails to overcome the requirement for separate expression (p. 8, paragraph 2).

Such is not persuasive. Under the modified basis applied, it is clear that the Art still makes the claims obvious.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, and Claim 19 remain rejected, and Claims 8, 11, and 18 are newly rejected, under 35 U.S.C. 103(a) as being unpatentable over US Pat. No. 5,540,926 to Aruffo, et al., and

US Pat. No. 6,207,456 to Baru, et al., as further evidenced by WO 04/042346 to Wohlgemuth, et al. and that attached SEQUENCE COMPARISON 1 OF 9/6/06, for reasons of record, as modified below due to the amendments.

As shown above, Aruffo teaches the various aspects of each claim. Moreover, Aruffo teaches that the protein may be grown in any mammalian cell (e.g., col. 7, paragraph 3). However, Aruffo does not teach the aspect of using a replication defective herpes virus vector.

On the other hand, Baru teaches liposome delivery systems for plasmids comprising heterologous inserts with improved efficiency in vitro (e.g., ABSTRACT; col. 1, last paragraph), and it is well known in the Art to make plasmids with separate expression elements directing expression of a selection marker in order to grow up the plasmids.

Hence, at the time of invention, it would have been obvious to modify the plasmid vectors of Aruffo with the liposome vectors of Baru to arrive at the claimed invention. The artisan would have been motivated to do so in order to produce vectors with improved efficiency, for producing pharmaceutical proteins. The Artisan would also have had a reasonable expectation of success, Aruffo had demonstrated the protein's production, and Baru had demonstrated the improved efficiency of such vector liposomes (EXAMPLES).

Response to Argument – Obviousness, Aruffo and Baru

Applicant's argument of 4/4/08 has been fully considered but is not found persuasive.

Applicant argues that the cited art fails to overcome the requirement for separate expression (p. 8, paragraph 2).

Such is not persuasive. Under the modified basis applied, it is clear that the Art still makes the claims obvious.

Bonyhadi Reference Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 5, and 19 remain rejected, and Claims 8-11 and 18 are newly rejected, under 35 U.S.C. 102(b) as being anticipated by Bonyhadi, et al. (1997) J. Virol., 71(6): 4707-16 for reasons of record and as necessitated by the amendments, below.

With regard to Claim 1, 4, 5, and 19, Bonyhadi teaches a nucleotide sequence comprising both a sequence encoding a therapeutic Rev mutant, and the mouse CD8-alpha gene sequence (e.g., FIGURE 2). Moreover, such sequences are operably linked to one or more transcriptional and translational regulatory sequences for their expression (e.g., the LTR and an IRES).

With regard to the amendments of Claims 4 and 5, requiring that the CD8-alpha chain consist essentially of the extracellular and transmembrane domains, it is noted that:

> By inclusion of the term "consisting essentially of" in the amended claim language, it appears that applicants have attempted to limit the CD8-alpha chain to exclude the intracellular domain. However, the specification does not define the use of the term "consisting essentially of". Still further, the essential characteristic of the CD8-alpha chain appears to be its ability to function as a veto molecule, which most preferably comprise such sequences (e.g., SPECIFICATION, paragraph 0011). Absent a clear indication in the specification or claims as to what is considered a material change in such basic and novel characteristics of "consisting essentially of", it will be construed as equivalent to "comprising" (see MPEP 2111.03). Therefore, a person of skill in the art would not have concluded that the claimed compositions are limited to only the extracellular and transmembrane domains.

With regard to Claims 8-11 and 18, the vector into which the nucleic acid is placed is an MMLV retroviral vector (e.g., p. 4708, cols. 1-2, paragraph bridging), which is further replication defective (e.g., Id., col. 2, paragraph 2). Moreover, the desired effects are necessarily obtained as the structure is met.

Lastly, with regard to separate expression, given the analysis of what is meant by separate expression, it appears that separate expression encompasses, in its broadest interpretation, a single transcript, which is translated separately, and such is shown to be anticipated here by the fact that an IRES is used for translation of the second gene (e.g., FIGURE 1).

Response to Argument – anticipation, Bonyhadi

Applicant's argument of 4/4/08 has been fully considered but is not found persuasive.

Applicant argues that the limitation "separately expressed" requires distinct transcripts, and hence, the claims are not anticipated (pp. 10-11).

Such is not persuasive. Separately expressed does not mean separately transcribed in the broadest reasonable interpretation of such limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 5, 7-11, and 18-30 remain and/or are newly rejected, under 35 U.S.C. 103(a) as being unpatentable over Zimmer, et al. (1999) Molecular Medicine 5(4): 244-53 and Bonyhadi, et al. (1997) J. Virol., 71(6): 4707-16, for reasons of record and as required by amendment below.

Zimmer teaches the administration of adenoviral vectors comprising the mouse or human ornithine carbamoyl transferase gene, for treatment of mice with OTC deficiency (ABSTRACT).

However, Zimmer does not teach the aspects of such adenoviral vector further comprising a CD8-alpha transgene.

On the other hand, Bonyhadi teaches that a second transgene encoding for CD8-alpha chain can be used for detection and/or enrichment of the transformation of the transduced cells (p. 4708, paragraph bridging columns). Further, as noted above, the CD8-alpha gene meets the requirements.

Hence, at the time of filing it would have been obvious to modify the methods of Zimmer with those of Bonyhadi, to arrive at an adenoviral vector comprising separately translated sequences for CD8-alpha, lacking its cytoplasmic tail, and for ornithine carbamoyl transferase. The Artisan would be motivated to do so to monitor and isolate the cells of Zimmer's transformed animals that were transformed, in order to study the amounts of ornithine carbamoyl transferase which was expressed, as taught by Zimmer. Moreover, the Artisan would have had a reasonable expectation of success, Zimmer had shown the method to work, and Bonyhadi had demonstrated that the cells' protein levels could be analyzed.

Response to Argument – Obviousness, Zimmer and Bonyhadi

Applicant's argument of 4/4/08 has been fully considered but is not found persuasive.

Applicant argues that Bonyhadi fails to teach or suggest separate transcripts, and hence, it cannot be used as art (pp. 11-12).

Such is not persuasive. Applicant's claims do not require separate transcripts, but only separate expression, which, as analyzed in the new matter rejection, above, is broad and generic as to what separate expression encompasses, and in its broadest reasonable interpretation would appear to the Artisan to encompass separate translations. Simply put, separate expression is not the same as separate transcripts.

Applicant argues that the new claims, by requiring the protein not to be a fusion protein, that the claims exclude bicistronic transcripts (pp. 12-13, paragraphs bridging).

Such is not persuasive. The proteins derived therefrom are not fusion proteins, and are derived from a bicistronic transcript in Bonyhadi. The Examiner requests further clarification.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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